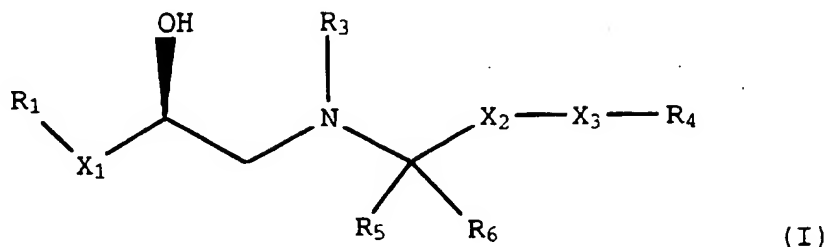


-109-

We claim:

1. A method of stimulating the  $\beta_3$  receptor which comprises administering to a patient in need thereof a compound of Formula I:

5



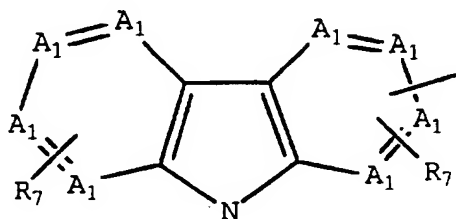
wherein:

X<sub>1</sub> is -OCH<sub>2</sub>-, -SCH<sub>2</sub>-, or a bond;

10 X<sub>2</sub> is a bond, or a 1 to 5 carbon straight or branched alkylene;

X<sub>3</sub> is O, S, or a bond;

R<sub>1</sub> is a fused heterocycle of the formula:



15

the A<sub>1</sub> groups are independently carbon or nitrogen, provided that no more than 2 nitrogens may be contained in either fused 6 membered ring and those 2 nitrogens may not be adjacent;

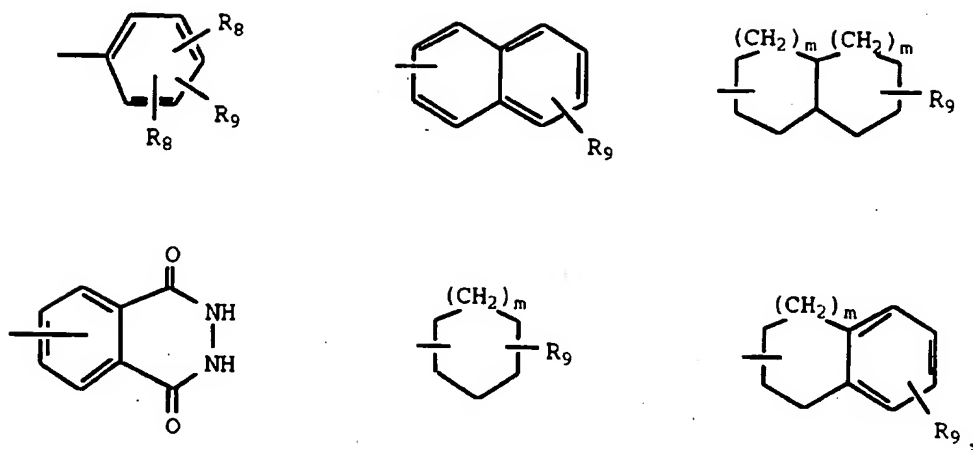
20 R<sub>2</sub> is independently hydrogen, C<sub>1</sub>-C<sub>4</sub> alkyl, or aryl;

R<sub>3</sub> is hydrogen or C<sub>1</sub>-C<sub>4</sub> alkyl;

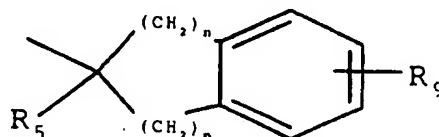
R<sub>4</sub> is an optionally substituted heterocycle or a moiety selected from the group consisting of:

25

-110-



- R5 is hydrogen or C1-C4 alkyl;  
 R6 is hydrogen, C1-C4 alkyl, or CO<sub>2</sub>(C1-C4 alkyl);  
 or R5 and R6 combine with the carbon to which each  
 is attached to form a C3-C6 cycloalkyl;  
 or R6 combines with X<sub>2</sub> and the carbon to which  
 each is attached to form a C3-C8 cycloalkyl;  
 or R6 combines with X<sub>2</sub>, R<sub>4</sub>, and the carbon to  
 which each is attached to form:



- provided that R<sub>5</sub> is hydrogen;  
 R<sub>7</sub> is independently hydrogen, halo, hydroxy, OR<sub>2</sub>,  
 C1-C4 alkyl, C1-C4 haloalkyl, aryl, COOR<sub>2</sub>, CONR<sub>2</sub>R<sub>2</sub>, NHCOR<sub>2</sub>,  
 C1-C4 alkoxy, NHR<sub>2</sub>, SR<sub>2</sub>, CN, SO<sub>2</sub>R<sub>2</sub>, SO<sub>2</sub>NHR<sub>2</sub>, or SOR<sub>2</sub>;  
 R<sub>8</sub> is independently hydrogen, halo, or C1-C4  
 alkyl;  
 R<sub>9</sub> is hydrogen, halo, hydroxy, CN, OR<sub>10</sub>, C1-C4  
 alkyl, C1-C4 haloalkyl, CO<sub>2</sub>R<sub>2</sub>, CONR<sub>11</sub>R<sub>12</sub>, CONH(C1-C4 alkyl  
 or C1-C4 alkoxy), SR<sub>2</sub>, CSNR<sub>2</sub>, CSNR<sub>11</sub>R<sub>12</sub>, NR<sub>2</sub>SO<sub>2</sub>R<sub>2</sub>, SO<sub>2</sub>R<sub>2</sub>,  
 SO<sub>2</sub>NR<sub>11</sub>R<sub>12</sub>, SOR<sub>2</sub>, NR<sub>11</sub>R<sub>12</sub>, optionally substituted aryl,  
 optionally substituted heterocycle, or C2-C4 alkenyl  
 substituted with CN, CO<sub>2</sub>R<sub>2</sub> or CONR<sub>11</sub>R<sub>12</sub>;

-111-

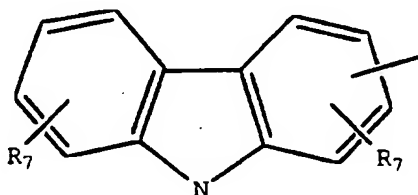
R<sub>10</sub> is C<sub>1</sub>-C<sub>4</sub> alkyl, C<sub>1</sub>-C<sub>4</sub> haloalkyl, (CH<sub>2</sub>)<sub>n</sub>C<sub>3</sub>-C<sub>8</sub> cycloalkyl, (CH<sub>2</sub>)<sub>n</sub>aryl, (CH<sub>2</sub>)<sub>n</sub>heterocycle, (CH<sub>2</sub>)<sub>n</sub>C<sub>3</sub>-C<sub>8</sub> optionally substituted cycloalkyl, (CH<sub>2</sub>)<sub>n</sub> optionally substituted aryl, (CH<sub>2</sub>)<sub>n</sub> optionally substituted heterocycle,  
5 or (CH<sub>2</sub>)<sub>n</sub>CO<sub>2</sub>R<sub>2</sub>;

R<sub>11</sub> and R<sub>12</sub> are independently hydrogen, C<sub>1</sub>-C<sub>4</sub> alkyl, aryl, (CH<sub>2</sub>)<sub>n</sub>aryl, or combine with the nitrogen to which each is bound to form morpholinyl, piperidinyl, pyrrolidinyl, or piperazinyl;

10 m is 0 or 1;

n is independently 0, 1, 2, or 3;  
or a pharmaceutically acceptable salt or solvate thereof.

15 2. The method of Claim 1 wherein R<sub>1</sub> is



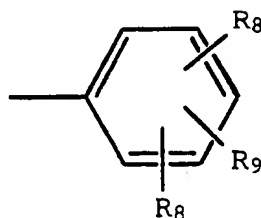
3. The method of Claim 2 wherein R<sub>7</sub> is hydrogen and R<sub>3</sub> is hydrogen.

20

4. The method of Claim 3 wherein X<sub>3</sub> is O or a bond.

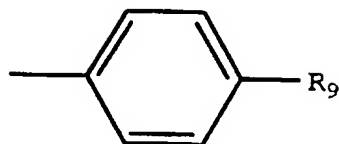
5. The method of Claim 4 wherein R<sub>5</sub> and R<sub>6</sub> are  
25 methyl, X<sub>2</sub> is methylene or ethylene, and X<sub>3</sub> is a bond.

6. The method of Claim 5 wherein R<sub>4</sub> is



-112-

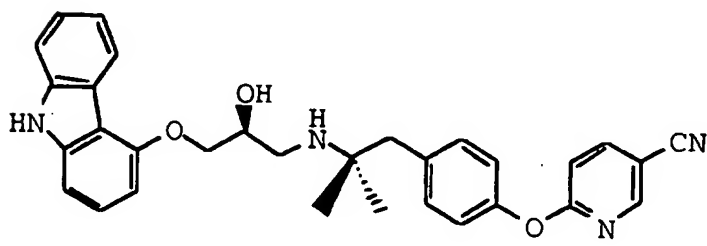
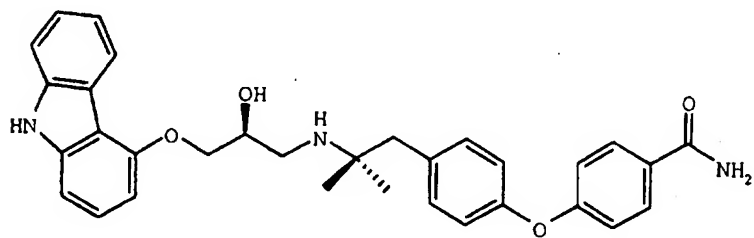
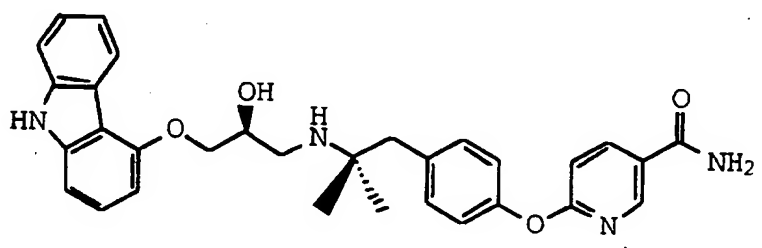
7. The method of Claim 6 wherein  $R_4$  is



5 and  $R_9$  is  $OR_{10}$  or  $NR_2SO_2R_2$ .

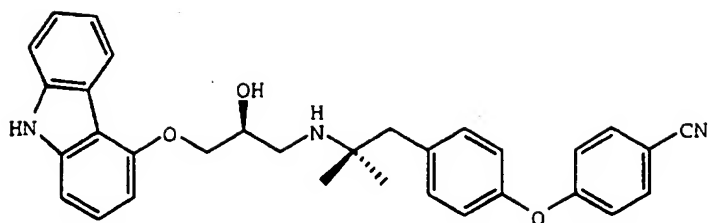
8. The method of Claim 7 wherein  $R_{10}$  is phenyl or pyridyl said phenyl or pyridyl being substituted with CN, hydroxy,  $CONR_{11}R_{12}$ ,  $CO_2R_2$ ,  $SO_2R_2$ , or  $SO_2NR_{11}R_{12}$ .

9. The method of Claim 8 wherein the compound is:

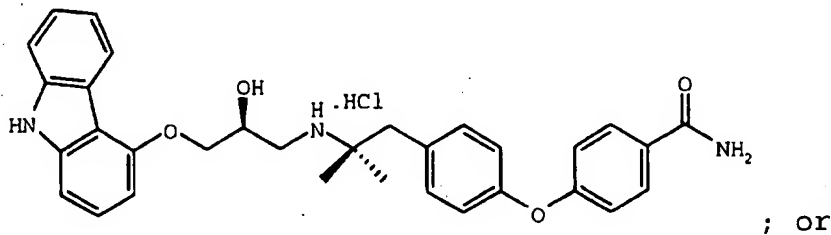


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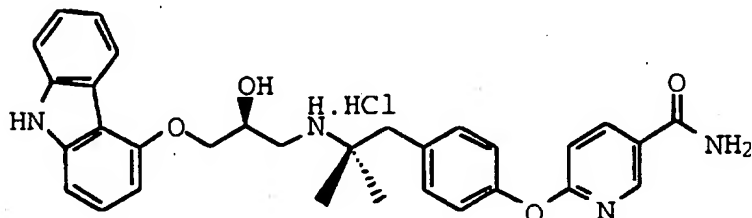
-113-



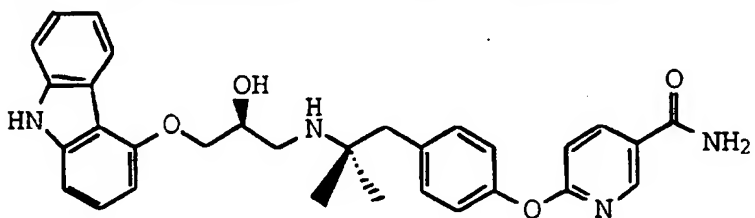
or a pharmaceutically acceptable salt or solvate thereof; or



5



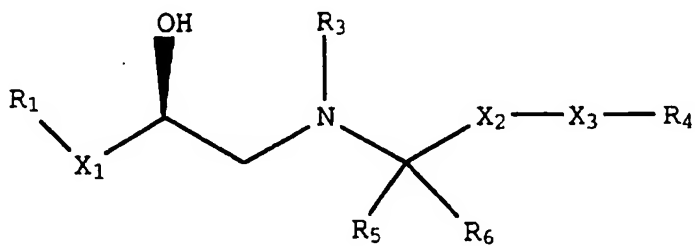
10. The method of claim 9 wherein the compound is



10 or a pharmaceutically acceptable salt or solvate.

11. A method of treating obesity which comprises administering to a patient in need thereof a compound of Formula I:

15



(I)

wherein:

-114-

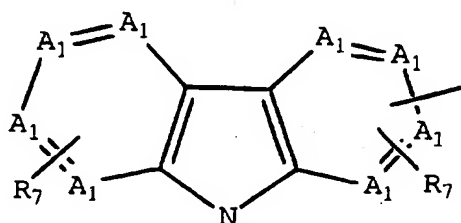
X<sub>1</sub> is -OCH<sub>2</sub>-, -SCH<sub>2</sub>-, or a bond;

X<sub>2</sub> is a bond, or a 1 to 5 carbon straight or branched alkylene;

X<sub>3</sub> is O, S, or a bond;

5

R<sub>1</sub> is a fused heterocycle of the formula:



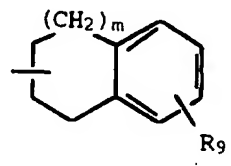
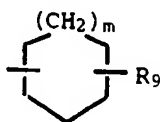
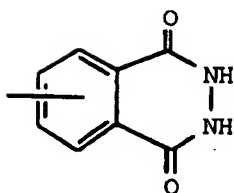
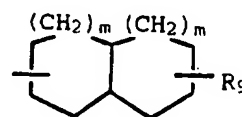
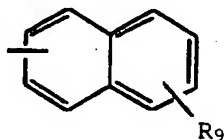
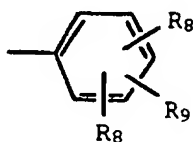
the A<sub>1</sub> groups are independently carbon or  
10 nitrogen, provided that no more than 2 nitrogens may be contained in either fused 6 membered ring and those 2 nitrogens may not be adjacent;

R<sub>2</sub> is independently hydrogen, C<sub>1</sub>-C<sub>4</sub> alkyl, or aryl;

15

R<sub>3</sub> is hydrogen or C<sub>1</sub>-C<sub>4</sub> alkyl;

R<sub>4</sub> is an optionally substituted heterocycle or a moiety selected from the group consisting of:



20

R<sub>5</sub> is hydrogen or C<sub>1</sub>-C<sub>4</sub> alkyl;

R<sub>6</sub> is hydrogen, C<sub>1</sub>-C<sub>4</sub> alkyl, or CO<sub>2</sub>(C<sub>1</sub>-C<sub>4</sub> alkyl);

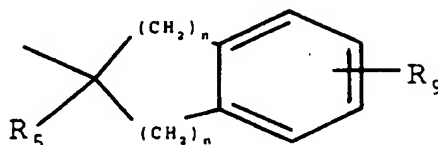
or R<sub>5</sub> and R<sub>6</sub> combine with the carbon to which each is attached to form a C<sub>3</sub>-C<sub>6</sub> cycloalkyl;

-115-

or R<sub>6</sub> combines with X<sub>2</sub> and the carbon to which each is attached to form a C<sub>3</sub>-C<sub>8</sub> cycloalkyl;

or R<sub>6</sub> combines with X<sub>2</sub>, R<sub>4</sub>, and the carbon to which each is attached to form:

5



provided that R<sub>5</sub> is hydrogen;

R<sub>7</sub> is independently hydrogen, halo, hydroxy, OR<sub>2</sub>, C<sub>1</sub>-C<sub>4</sub> alkyl, C<sub>1</sub>-C<sub>4</sub> haloalkyl, aryl, COOR<sub>2</sub>, CONR<sub>2</sub>R<sub>2</sub>, NHCOR<sub>2</sub>,  
 10 C<sub>1</sub>-C<sub>4</sub> alkoxy, NHR<sub>2</sub>, SR<sub>2</sub>, CN, SO<sub>2</sub>R<sub>2</sub>, SO<sub>2</sub>NHR<sub>2</sub>, or SOR<sub>2</sub>;

R<sub>8</sub> is independently hydrogen, halo, or C<sub>1</sub>-C<sub>4</sub> alkyl;

R<sub>9</sub> is hydrogen, halo, hydroxy, CN, OR<sub>10</sub>, C<sub>1</sub>-C<sub>4</sub> alkyl, C<sub>1</sub>-C<sub>4</sub> haloalkyl, CO<sub>2</sub>R<sub>2</sub>, CONR<sub>11</sub>R<sub>12</sub>, CONH(C<sub>1</sub>-C<sub>4</sub> alkyl  
 15 or C<sub>1</sub>-C<sub>4</sub> alkoxy), SR<sub>2</sub>, CSNR<sub>2</sub>, CSNR<sub>11</sub>R<sub>12</sub>, NR<sub>2</sub>SO<sub>2</sub>R<sub>2</sub>, SO<sub>2</sub>R<sub>2</sub>, SO<sub>2</sub>NR<sub>11</sub>R<sub>12</sub>, SOR<sub>2</sub>, NR<sub>11</sub>R<sub>12</sub>, optionally substituted aryl, optionally substituted heterocycle, or C<sub>2</sub>-C<sub>4</sub> alkenyl substituted with CN, CO<sub>2</sub>R<sub>2</sub> or CONR<sub>11</sub>R<sub>12</sub>;

R<sub>10</sub> is C<sub>1</sub>-C<sub>4</sub> alkyl, C<sub>1</sub>-C<sub>4</sub> haloalkyl, (CH<sub>2</sub>)<sub>n</sub>C<sub>3</sub>-C<sub>8</sub>  
 20 cycloalkyl, (CH<sub>2</sub>)<sub>n</sub>aryl, (CH<sub>2</sub>)<sub>n</sub>heterocycle, (CH<sub>2</sub>)<sub>n</sub>C<sub>3</sub>-C<sub>8</sub> optionally substituted cycloalkyl, (CH<sub>2</sub>)<sub>n</sub> optionally substituted aryl, (CH<sub>2</sub>)<sub>n</sub> optionally substituted heterocycle, or (CH<sub>2</sub>)<sub>n</sub>CO<sub>2</sub>R<sub>2</sub>;

R<sub>11</sub> and R<sub>12</sub> are independently hydrogen, C<sub>1</sub>-C<sub>4</sub>  
 25 alkyl, aryl, (CH<sub>2</sub>)<sub>n</sub>aryl, or combine with the nitrogen to which each is bound to form morpholinyl, piperidinyl, pyrrolidinyl, or piperazinyl;

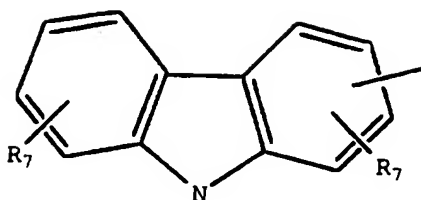
m is 0 or 1;

n is independently 0, 1, 2, or 3;

30 or a pharmaceutically acceptable salt or solvate thereof.

12. The method of Claim 11 wherein R<sub>1</sub> is

-116-



13. The method of Claim 12 wherein  $R_7$  is hydrogen and  $R_3$  is hydrogen.

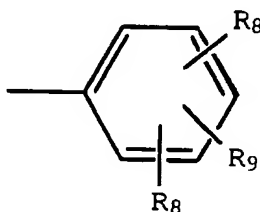
5

14. The method of Claim 13 wherein  $X_3$  is O or a bond.

15. The method of Claim 14 wherein  $R_5$  and  $R_6$  are methyl,  $X_2$  is methylene or ethylene, and  $X_3$  is a bond.

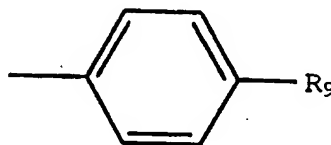
10

16. The method of Claim 15 wherein  $R_4$  is



15

17. The method of Claim 16 wherein  $R_4$  is



and  $R_9$  is  $OR_{10}$  or  $NR_2SO_2R_2$ .

20

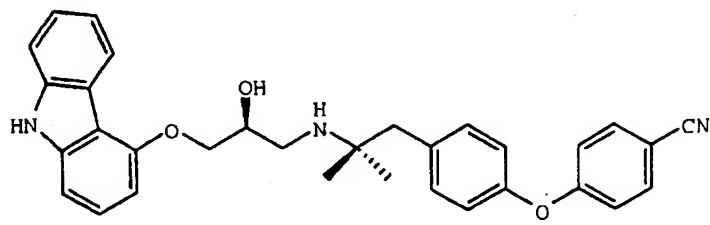
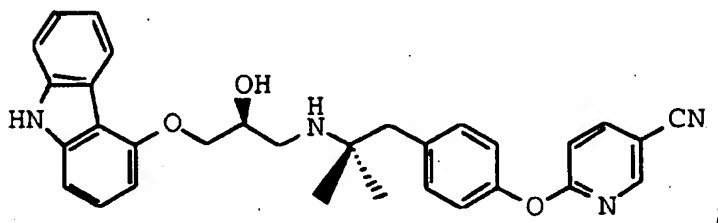
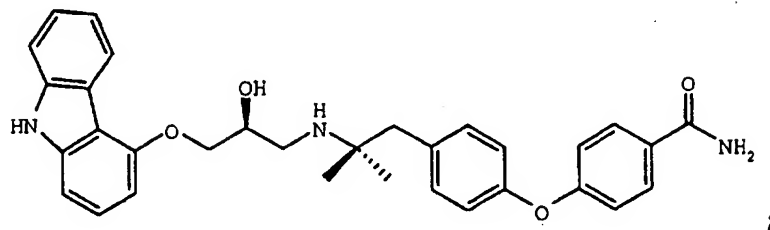
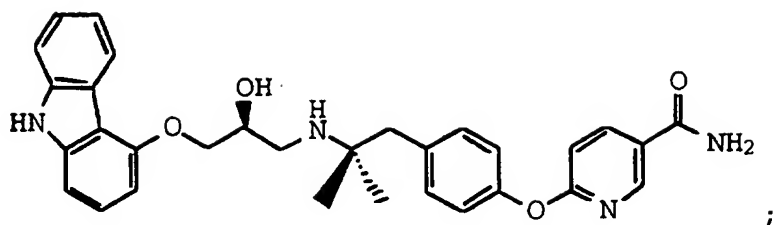
18. The method of Claim 17 wherein  $R_{10}$  is phenyl or pyridyl said phenyl or pyridyl being substituted with CN, hydroxy,  $CONR_{11}R_{12}$ ,  $CO_2R_2$ ,  $SO_2R_2$ , or  $SO_2NR_{11}R_{12}$ .

25

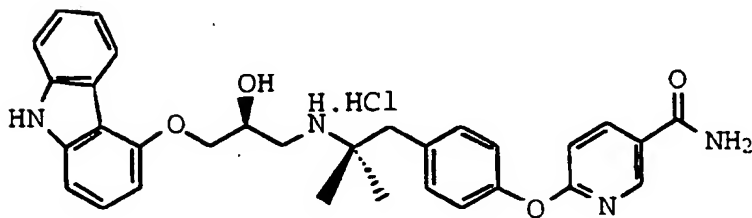
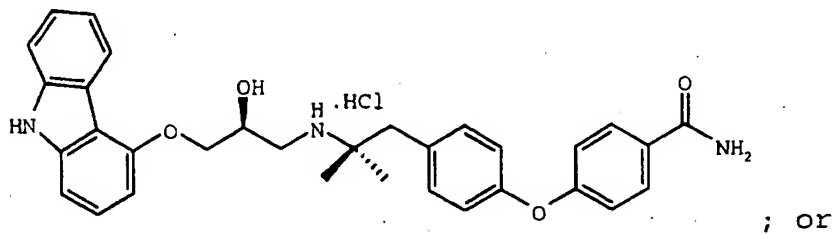
19. The method of Claim 18 wherein the compound is:



-117-

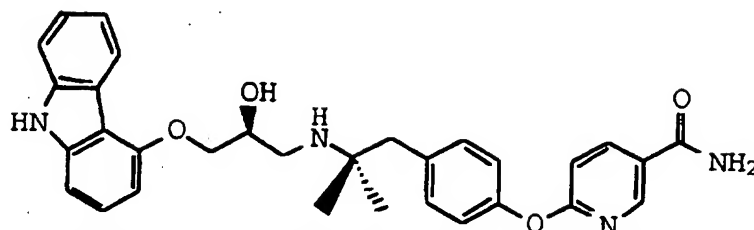


or a pharmaceutically acceptable salt or solvate thereof; or



-118-

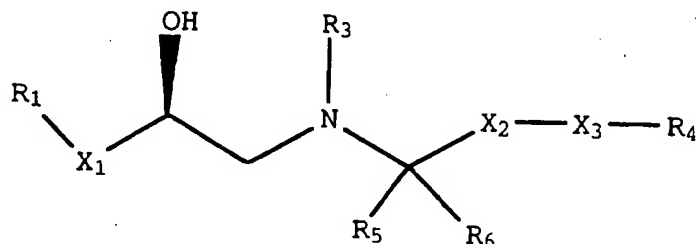
20. The method of claim 19 wherein the compound  
is



or a pharmaceutically acceptable salt or solvate thereof.

5

21. A method of treating Type II diabetes which  
comprises administering to a patient in need thereof a  
compound of Formula I:



10

(I)

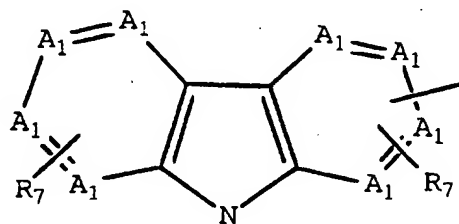
wherein:

X<sub>1</sub> is -OCH<sub>2</sub>-, -SCH<sub>2</sub>-, or a bond;

X<sub>2</sub> is a bond, or a 1 to 5 carbon straight or  
branched alkylene;

15 X<sub>3</sub> is O, S, or a bond;

R<sub>1</sub> is a fused heterocycle of the formula:



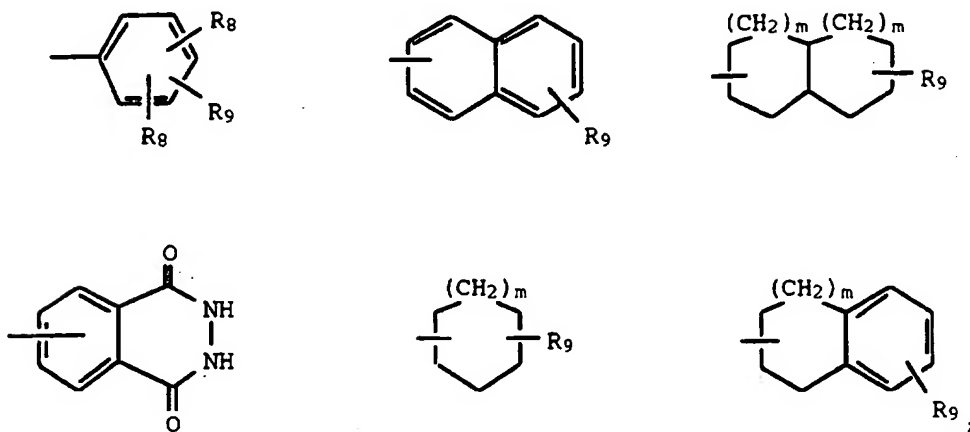
20 the A<sub>1</sub> groups are independently carbon or  
nitrogen, provided that no more than 2 nitrogens may be  
contained in either fused 6 membered ring and those 2  
nitrogens may not be adjacent;

25 R<sub>2</sub> is independently hydrogen, C<sub>1</sub>-C<sub>4</sub> alkyl, or  
aryl;

R<sub>3</sub> is hydrogen or C<sub>1</sub>-C<sub>4</sub> alkyl;

-119-

R<sub>4</sub> is an optionally substituted heterocycle or a moiety selected from the group consisting of:



5

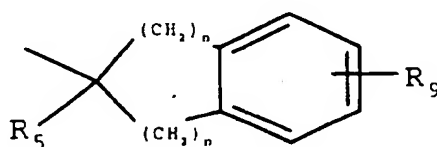
R<sub>5</sub> is hydrogen or C<sub>1</sub>-C<sub>4</sub> alkyl;

R<sub>6</sub> is hydrogen, C<sub>1</sub>-C<sub>4</sub> alkyl, or CO<sub>2</sub>(C<sub>1</sub>-C<sub>4</sub> alkyl);

or R<sub>5</sub> and R<sub>6</sub> combine with the carbon to which each is attached to form a C<sub>3</sub>-C<sub>6</sub> cycloalkyl;

10 or R<sub>6</sub> combines with X<sub>2</sub> and the carbon to which each is attached to form a C<sub>3</sub>-C<sub>8</sub> cycloalkyl;

or R<sub>6</sub> combines with X<sub>2</sub>, R<sub>4</sub>, and the carbon to which each is attached to form:



15

provided that R<sub>5</sub> is hydrogen;

R<sub>7</sub> is independently hydrogen, halo, hydroxy, OR<sub>2</sub>, C<sub>1</sub>-C<sub>4</sub> alkyl, C<sub>1</sub>-C<sub>4</sub> haloalkyl, aryl, COOR<sub>2</sub>, CONR<sub>2</sub>R<sub>2</sub>, NHCOR<sub>2</sub>, C<sub>1</sub>-C<sub>4</sub> alkoxy, NHR<sub>2</sub>, SR<sub>2</sub>, CN, SO<sub>2</sub>R<sub>2</sub>, SO<sub>2</sub>NHR<sub>2</sub>, or SOR<sub>2</sub>;

20 R<sub>8</sub> is independently hydrogen, halo, or C<sub>1</sub>-C<sub>4</sub> alkyl;

R<sub>9</sub> is hydrogen, halo, hydroxy, CN, OR<sub>10</sub>, C<sub>1</sub>-C<sub>4</sub> alkyl, C<sub>1</sub>-C<sub>4</sub> haloalkyl, CO<sub>2</sub>R<sub>2</sub>, CONR<sub>11</sub>R<sub>12</sub>, CONH(C<sub>1</sub>-C<sub>4</sub> alkyl or C<sub>1</sub>-C<sub>4</sub> alkoxy), SR<sub>2</sub>, CSNR<sub>2</sub>, CSNR<sub>11</sub>R<sub>12</sub>, NR<sub>2</sub>SO<sub>2</sub>R<sub>2</sub>, SO<sub>2</sub>R<sub>2</sub>,

25 SO<sub>2</sub>NR<sub>11</sub>R<sub>12</sub>, SOR<sub>2</sub>, NR<sub>11</sub>R<sub>12</sub>, optionally substituted aryl,

- 120 -

optionally substituted heterocycle, or C<sub>2</sub>-C<sub>4</sub> alkenyl substituted with CN, CO<sub>2</sub>R<sub>2</sub> or CONR<sub>11</sub>R<sub>12</sub>;

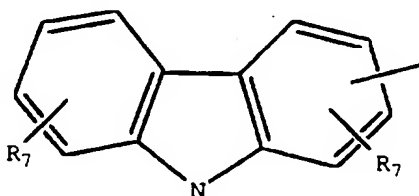
R<sub>10</sub> is C<sub>1</sub>-C<sub>4</sub> alkyl, C<sub>1</sub>-C<sub>4</sub> haloalkyl, (CH<sub>2</sub>)<sub>n</sub>C<sub>3</sub>-C<sub>8</sub> cycloalkyl, (CH<sub>2</sub>)<sub>n</sub>aryl, (CH<sub>2</sub>)<sub>n</sub>heterocycle, (CH<sub>2</sub>)<sub>n</sub>C<sub>3</sub>-C<sub>8</sub> optionally substituted cycloalkyl, (CH<sub>2</sub>)<sub>n</sub> optionally substituted aryl, (CH<sub>2</sub>)<sub>n</sub> optionally substituted heterocycle, or (CH<sub>2</sub>)<sub>n</sub>CO<sub>2</sub>R<sub>2</sub>;

R<sub>11</sub> and R<sub>12</sub> are independently hydrogen, C<sub>1</sub>-C<sub>4</sub> alkyl, aryl, (CH<sub>2</sub>)<sub>n</sub>aryl, or combine with the nitrogen to which each is bound to form morpholinyl, piperidinyl, pyrrolidinyl, or piperazinyl;

m is 0 or 1;

n is independently 0, 1, 2, or 3;  
or a pharmaceutically acceptable salt or solvate thereof.

22. The method of Claim 21 wherein R<sub>1</sub> is



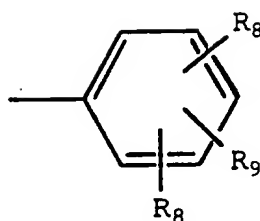
23. The method of Claim 22 wherein R<sub>7</sub> is hydrogen and R<sub>3</sub> is hydrogen.

24. The method of Claim 23 wherein X<sub>3</sub> is O or a bond.

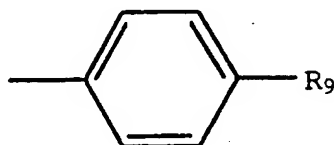
25. The method of Claim 24 wherein R<sub>5</sub> and R<sub>6</sub> are methyl, X<sub>2</sub> is methylene or ethylene, and X<sub>3</sub> is a bond.

26. The method of Claim 25 wherein R<sub>4</sub> is

-121-



27. The method of Claim 26 wherein  $R_4$  is



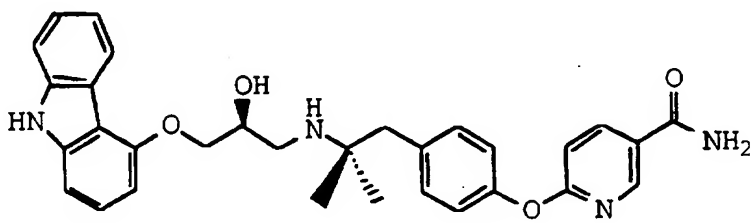
5

and  $R_9$  is  $OR_{10}$  or  $NR_2SO_2R_2$ .

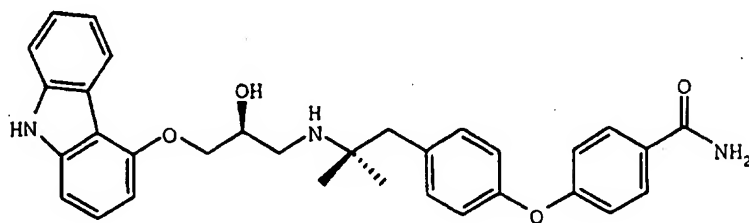
28. The method of Claim 27 wherein  $R_{10}$  is phenyl or pyridyl said phenyl or pyridyl being substituted with CN, hydroxy,  $CONR_{11}R_{12}$ ,  $CO_2R_2$ ,  $SO_2R_2$ , or  $SO_2NR_{11}R_{12}$ .

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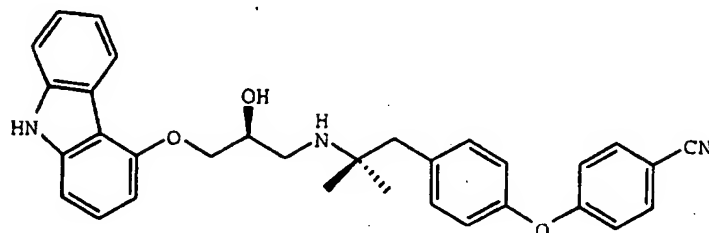
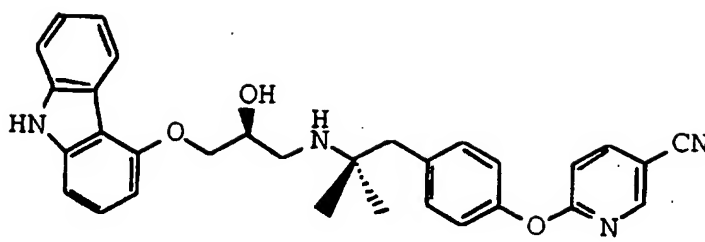
29. The method of Claim 28 wherein the compound is:



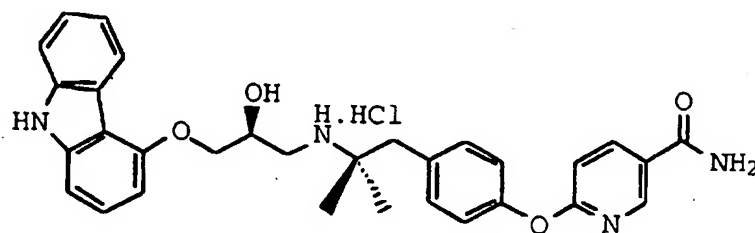
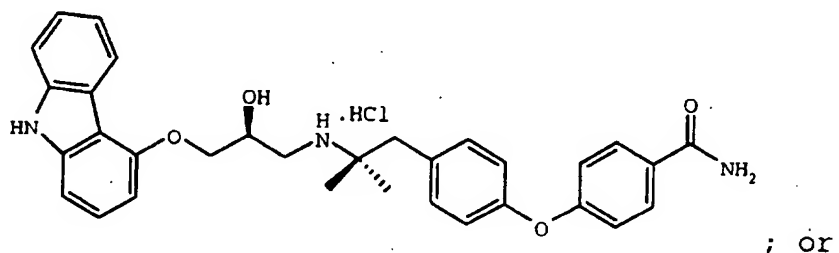
15



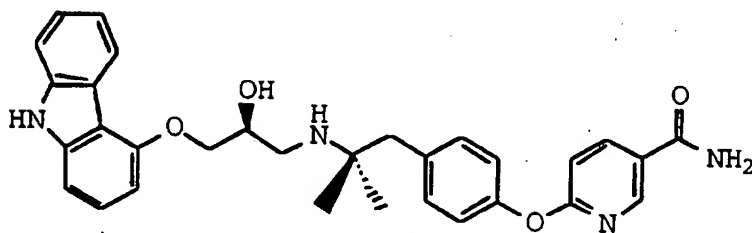
-122-



or a pharmaceutically acceptable salt or solvate thereof; or



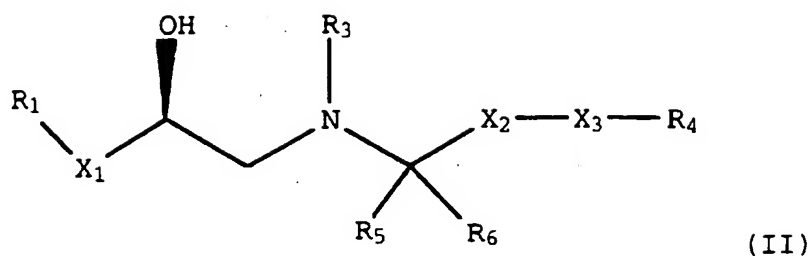
30. The method of claim 29 wherein the compound



or a pharmaceutically acceptable salt or solvate.

31. A compound of the Formula II

-123-

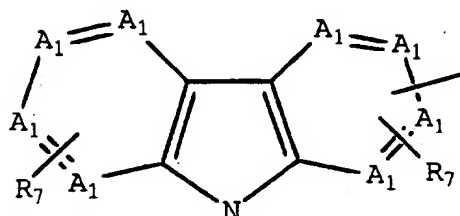


wherein:

X<sub>1</sub> is -OCH<sub>2</sub>-, -SCH<sub>2</sub>-, or a bond;

X<sub>3</sub> is O, S, or a bond;

5 R<sub>1</sub> is a fused heterocycle of the formula:



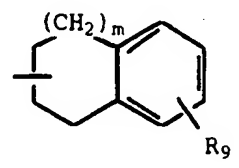
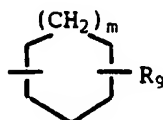
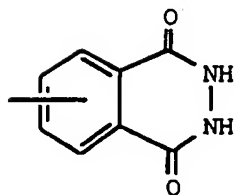
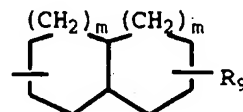
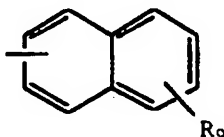
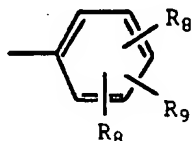
the A<sub>1</sub> groups of said heterocycle are

10 independently carbon or nitrogen, provided that no more than 2 nitrogens may be contained in either fused 6 membered ring and those 2 nitrogens may not be adjacent;

R<sub>2</sub> is independently hydrogen, C<sub>1</sub>-C<sub>4</sub> alkyl, or aryl;

15 R<sub>3</sub> is hydrogen or C<sub>1</sub>-C<sub>4</sub> alkyl;

R<sub>4</sub> is an optionally substituted heterocycle or a moiety selected from the group consisting of:



-124-

X<sub>2</sub> is a bond, or a 1 to 5 carbon straight or branched alkylene;

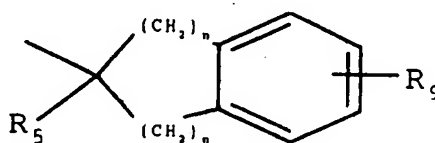
R<sub>5</sub> is hydrogen or C<sub>1</sub>-C<sub>4</sub> alkyl;

R<sub>6</sub> is hydrogen, C<sub>1</sub>-C<sub>4</sub> alkyl, or CO<sub>2</sub>(C<sub>1</sub>-C<sub>4</sub> alkyl);

5 or R<sub>5</sub> and R<sub>6</sub> combine with the carbon to which each is attached to form a C<sub>3</sub>-C<sub>6</sub> cycloalkyl;

or R<sub>6</sub> combines with X<sub>2</sub> and the carbon to which each is attached to form a C<sub>3</sub>-C<sub>8</sub> cycloalkyl;

10 or R<sub>6</sub> combines with X<sub>2</sub>, R<sub>4</sub>, and the carbon to which each is attached to form:



provided that R<sub>5</sub> is hydrogen;

15 R<sub>7</sub> is independently hydrogen, halo, hydroxy, OR<sub>2</sub>, C<sub>1</sub>-C<sub>4</sub> alkyl, C<sub>1</sub>-C<sub>4</sub> haloalkyl, aryl, COOR<sub>2</sub>, CONHR<sub>2</sub>, NHCOR<sub>2</sub>, C<sub>1</sub>-C<sub>4</sub> alkoxy, NHR<sub>2</sub>, SR<sub>2</sub>, CN, SO<sub>2</sub>R<sub>2</sub>, SO<sub>2</sub>NHR<sub>2</sub>, or SOR<sub>2</sub>;

R<sub>8</sub> is independently hydrogen, halo or C<sub>1</sub>-C<sub>4</sub> alkyl;

20 R<sub>9</sub> is halo, CN, OR<sub>10</sub>, C<sub>1</sub>-C<sub>4</sub> alkyl, C<sub>1</sub>-C<sub>4</sub> haloalkyl, CO<sub>2</sub>R<sub>2</sub>, CONR<sub>11</sub>R<sub>12</sub>, CONH(C<sub>1</sub>-C<sub>4</sub> alkyl or C<sub>1</sub>-C<sub>4</sub> alkoxy), SR<sub>2</sub>, CSNR<sub>2</sub>, CSNR<sub>11</sub>R<sub>12</sub>, NR<sub>2</sub>SO<sub>2</sub>R<sub>2</sub>, SO<sub>2</sub>R<sub>2</sub>, SO<sub>2</sub>NR<sub>11</sub>R<sub>12</sub>, SOR<sub>2</sub>, NR<sub>11</sub>R<sub>12</sub>, optionally substituted aryl, optionally substituted heterocycle, or C<sub>2</sub>-C<sub>4</sub> alkenyl substituted with CN, CO<sub>2</sub>R<sub>2</sub> or CONR<sub>11</sub>R<sub>12</sub>;

25 R<sub>10</sub> is C<sub>1</sub>-C<sub>4</sub> alkyl, C<sub>1</sub>-C<sub>4</sub> haloalkyl, (CH<sub>2</sub>)<sub>n</sub>C<sub>3</sub>-C<sub>8</sub> cycloalkyl, (CH<sub>2</sub>)<sub>n</sub>aryl, (CH<sub>2</sub>)<sub>n</sub>heterocycle, (CH<sub>2</sub>)<sub>n</sub>C<sub>3</sub>-C<sub>8</sub> optionally substituted cycloalkyl, (CH<sub>2</sub>)<sub>n</sub> optionally substituted aryl, (CH<sub>2</sub>)<sub>n</sub> optionally substituted heterocycle, or (CH<sub>2</sub>)<sub>n</sub>CO<sub>2</sub>R<sub>2</sub>;

30 R<sub>11</sub> and R<sub>12</sub> are independently hydrogen, C<sub>1</sub>-C<sub>4</sub> alkyl, aryl, (CH<sub>2</sub>)<sub>n</sub>aryl, or combine with the nitrogen to which each is bound to form morpholinyl, piperidinyl, pyrrolidinyl, or piperazinyl;

m is 0 or 1;

n is independently 0, 1, 2, or 3;



-125-

provided:

when  $R_5$  or  $R_6$  is hydrogen; either1) one or more  $A_1$  must be nitrogen,

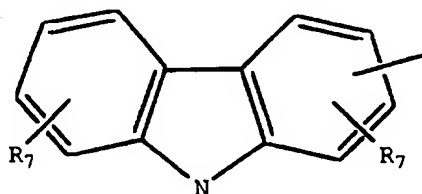
or

- 5           2)  $R_9$  is CN,  $OR_{10}$ ,  $CO_2R_2$ ,  $CSNR_2$ ,  $CSNR_{11}R_{12}$ ,  
 $NR_2SO_2R_2$ ,  $SO_2NR_{11}R_{12}$ , optionally substituted aryl,  
 optionally substituted heterocycle, or C<sub>2</sub>-C<sub>4</sub> alkenyl  
 substituted with CN,  $CO_2R_2$  or  $CONR_{11}R_{12}$ ; and

- 10            $R_{10}$  is C<sub>1</sub>-C<sub>4</sub> haloalkyl,  $(CH_2)_n$ C<sub>3</sub>-C<sub>8</sub> cycloalkyl,  
 $(CH_2)_n$ heterocycle,  $(CH_2)_n$ C<sub>3</sub>-C<sub>8</sub> optionally substituted  
 cycloalkyl,  $(CH_2)_n$  optionally substituted aryl, or  $(CH_2)_n$   
 optionally substituted heterocycle;  
 or a pharmaceutically acceptable salt or solvate thereof.

- 15           32. A compound of Claim 31 wherein  $R_5$  and  $R_6$  are  
 methyl or ethyl.

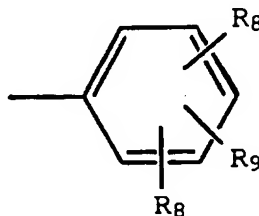
33. A compound of Claim 32 wherein  $R_1$  is



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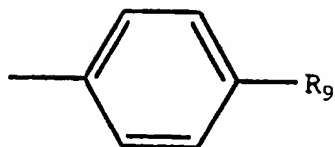
34. A compound of Claim 33 wherein  $X_2$  is  
 methylene or ethylene.

- 25           35. A compound of Claim 34 wherein  $R_4$  is



36. A compound of Claim 35 wherein  $R_4$  is

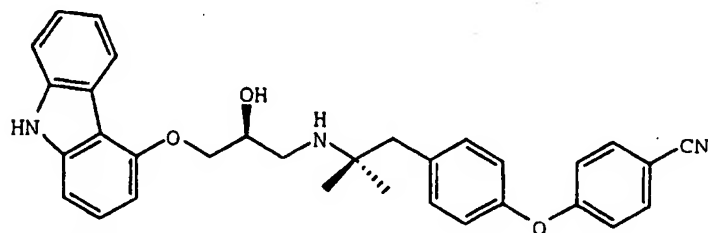
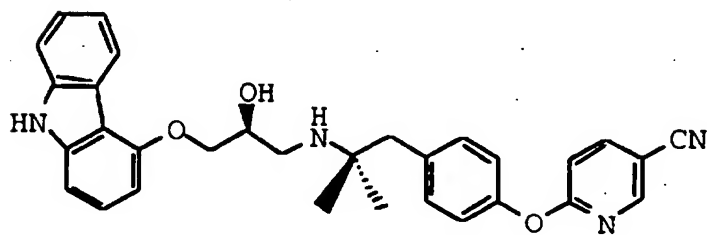
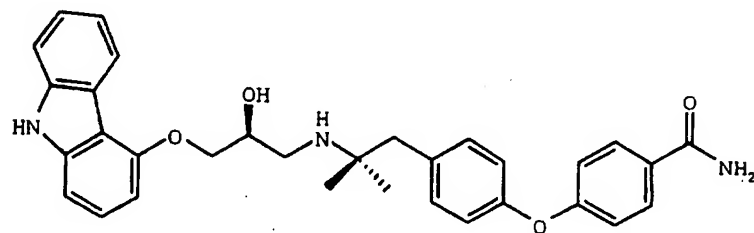
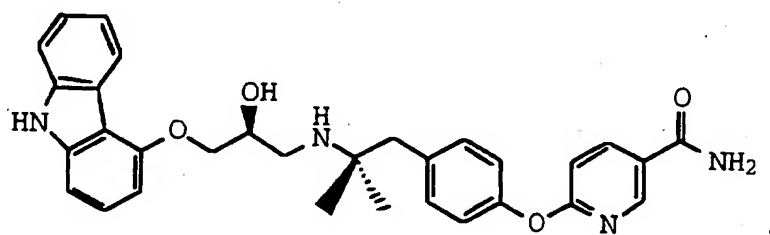
-126-



and  $R_9$  is  $OR_{10}$  or  $NR_2SO_2R_2$ .

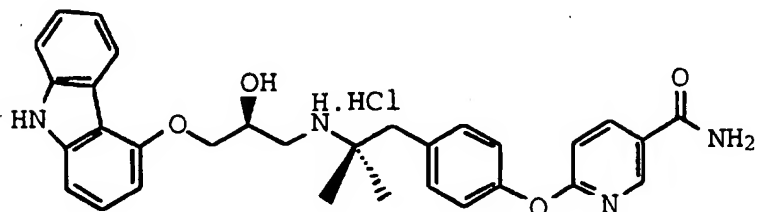
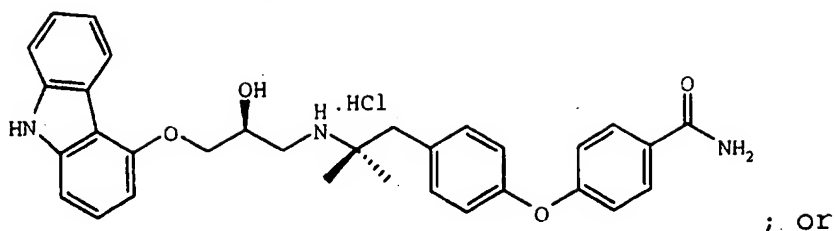
5 37. A compound of Claim 36 wherein  $R_{10}$  is phenyl or pyridyl said phenyl or pyridyl being substituted with CN,  $CONR_{11}R_{12}$ ,  $CO_2R_2$ ,  $SO_2R_2$ , or  $SO_2NR_{11}R_{12}$ .

10 38. A compound of Claim 37 which is:

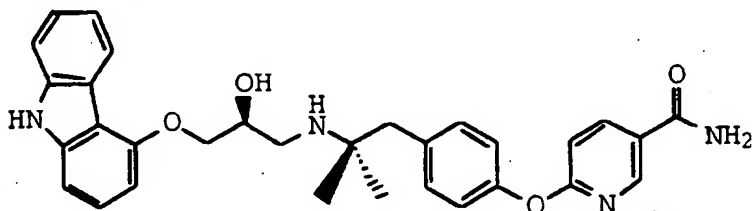


15 or a pharmaceutically acceptable salt or solvate thereof; or

- 127 -



39. The compound of claim 38 of the formula



or a pharmaceutically acceptable salt or solvate.

40. A pharmaceutical formulation comprising as an active ingredient a compound of Claim 31, associated with one or more pharmaceutically acceptable carriers, excipients or diluents.

41. A pharmaceutical formulation comprising as an active ingredient a compound of Claim 32, associated with one or more pharmaceutically acceptable carriers, excipients or diluents.

42. A pharmaceutical formulation comprising as an active ingredient a compound of Claim 33, associated with one or more pharmaceutically acceptable carriers, excipients or diluents.

- 128 -

43. A pharmaceutical formulation comprising as an active ingredient a compound of Claim 34, associated with one or more pharmaceutically acceptable carriers, excipients or diluents.

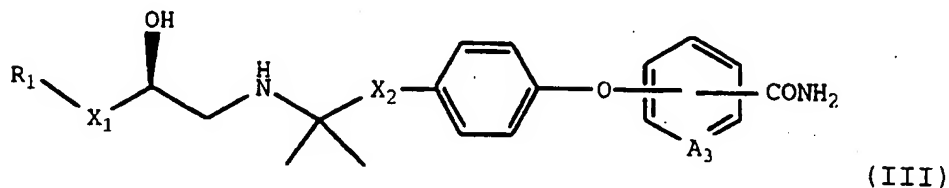
44. A pharmaceutical formulation comprising as an active ingredient a compound of Claim 35, associated with one or more pharmaceutically acceptable carriers, excipients or diluents.

45. A pharmaceutical formulation comprising as an active ingredient a compound of Claim 36, associated with one or more pharmaceutically acceptable carriers, excipients or diluents.

46. A pharmaceutical formulation comprising as an active ingredient a compound of Claim 38, associated with one or more pharmaceutically acceptable carriers, excipients or diluents.

47. A pharmaceutical formulation comprising as an active ingredient a compound of Claim 39, associated with one or more pharmaceutically acceptable carriers, excipients or diluents.

48. A process of preparing a compound of claim 31 of the formula III:



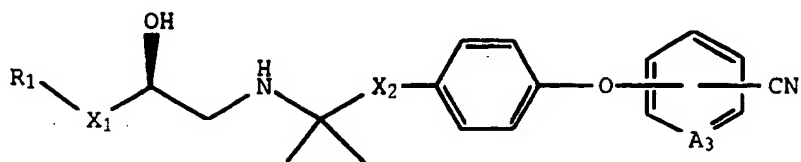
wherein:

A<sub>3</sub> is CH or N;

- 129 -

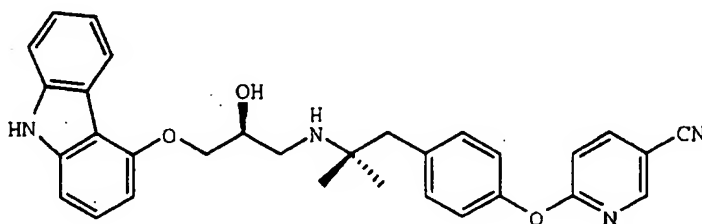
which comprises:

in step 1, hydrolysis of a compound of the formula:



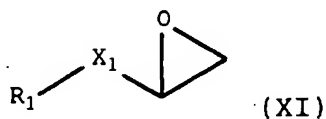
and optionally in step 2, reacting the product of step 1 with an acid to form an acid addition salt.

49. The process of claim 48 wherein in step 1 the hydrolysis is of a compound of the formula

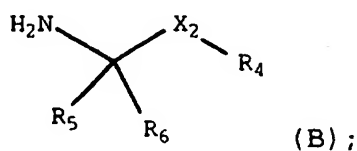


50. A process of preparing a compound of Claim 31, which comprises:

in step 1, reacting an epoxide of the formula XI:



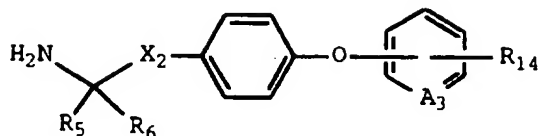
with an amine of formula B:



and optionally in step 2, reacting the product of step 1 with an acid to form an acid addition salt.

- 130 -

51. A process of Claim 50, wherein the amine is of the formula:



wherein:

A<sub>3</sub> is CH or N;

R<sub>14</sub> is C<sub>1</sub>-C<sub>4</sub> alkyl, C<sub>1</sub>-C<sub>4</sub> haloalkyl, hydroxy, carboxy, tetrazolyl, acyl, COOR<sub>2</sub>, CONR<sub>11</sub>R<sub>12</sub>, CONH(C<sub>1</sub>-C<sub>4</sub> alkoxy), cyano, C<sub>1</sub>-C<sub>4</sub> alkoxy, C<sub>1</sub>-C<sub>4</sub> alkyl, phenyl, nitro, NR<sub>11</sub>R<sub>12</sub>, NHCO(C<sub>1</sub>-C<sub>4</sub> alkyl), NHCO(benzyl), NHCO(phenyl), SR<sub>2</sub>, S(C<sub>1</sub>-C<sub>4</sub> alkyl), OCO(C<sub>1</sub>-C<sub>4</sub> alkyl), SO<sub>2</sub>(NR<sub>11</sub>R<sub>12</sub>), SO<sub>2</sub>(C<sub>1</sub>-C<sub>4</sub> alkyl), or SO<sub>2</sub>(phenyl).

52. The process of claim 50 wherein;

A<sub>3</sub> is N; and

R<sub>14</sub> is COOR<sub>2</sub>, CONR<sub>11</sub>R<sub>12</sub>, CONH(C<sub>1</sub>-C<sub>4</sub> alkoxy), or cyano.